Relaxation Time Measurements of Bone Marrow Protons in the Calcaneus Using a Compact MRI System at 0.2 Tesla Field Strength

Sadanori Tomiha, Nachiko Iita, Fumi Okada, Shinya Handa, and Katsumi Kose*

Relaxation times (T₁ and T₂) of the bone marrow protons and trabecular bone volume fraction (TBVF) in the calcaneus were measured for 100 female volunteers using a compact MRI system at 0.2 T field strength. The speed of sound (SOS) through the calcaneus was measured also for the same subjects using a quantitative ultrasound system. Both relaxation times were found to have positive correlations with age (R = 0.40; P < 0.0001 and R = 0.31; P < 0.002, respectively) and negative correlations with SOS (R = −0.38; P < 0.0001 and R = −0.36; P < 0.0001, respectively). Although TBVF had a fairly high positive correlation with the SOS (R = 0.67), neither T₁ nor T₂ were correlated with TBVF (R = −0.062 and −0.024, respectively). These results suggest that the age dependence of both T₁ and T₂ is caused by the microdynamic properties of the lipid molecules in bone marrow observed using acoustic or elastic modalities. Magn Reson Med 60:485–488, 2008. © 2008 Wiley-Liss, Inc.

Key words: osteoporosis; trabecular bone; bone marrow; relaxation time; calcaneus

Bone density measurements using dual-energy X-ray absorptiometry (DXA) and quantitative ultrasound (QUS) are widely used for diagnosis and the assessment of drug therapy for osteoporosis. DXA is a transmission method for measuring areal bone mineral density (BMD) by correcting soft tissue absorption using two different energy X-ray beams. QUS is also a transmission method through a bulk tissue (mostly the heel) in which speed of sound (SOS) and other acoustic parameters such as the frequency dependence of sound attenuation are measured.

Bone density measurements using MRI have several advantages over the above conventional methods. MRI can measure the “volume” density of trabecular bone (TB), which is much more sensitive to bone metabolism than cortical bone. Furthermore, unlike DXA, MRI does not use ionizing radiation and provides a much clearer physical interpretation of the measured results than QUS.

Three different MRI approaches to bone density measurement have been proposed (1–9). The first is based on high resolution MRI, which can spatially resolve TB from bone marrow. This also provides a measure of TB microstructure, which gives useful information on TB strength (1–4). The second approach is based on measuring the relaxation rate Rₛ of transverse nuclear magnetization arising from the difference in susceptibility between TB and bone marrow (5–7). The third approach is based on quantification of bone marrow protons in a voxel, which is a complementary quantity of TB volume fraction (TBVF) in a voxel (8,9).

Because the first and second approaches need a high magnetic field strength (> 1.0 Tesla [T]), we used the third method to construct a compact MRI system for measuring TBVF in the calcaneus (10). A particular advantage of the system is that it can measure TBVF in the calcaneus in a few minutes, thereby allowing the rapid scanning of many subjects. We measured the relaxation times of bone marrow protons, TBVF, and SOS for the calcaneus of 100 female volunteers to clarify the NMR properties of bone marrow protons.

**MATERIALS AND METHODS**

One male (age 51 years) and 100 female volunteers (age range 16–81, mean 42.5 ± 17.7 years) participated in this study. The women reported no specific bone related disease before the measurements. After written informed consent was received, MRI and QUS measurements were performed at the right calcaneus of the women. The male subject’s right calcaneus was used for 10-minute serial MRI measurements after his right foot had been cooled in ice water for approximately 15 minutes.

A compact dedicated MRI system with a 0.21T and 16 cm gap permanent magnet developed in our laboratory was used for MRI measurements (10). The MRI system comprised the permanent magnet, a gradient coil set, a radiofrequency (RF) probe, and a portable MRI console. The RF coil was a nine-turn solenoid with an oval aperture (long axis = 170 mm, short axis = 90 mm, length = 100 mm) optimized for heel imaging (11). Two cylindrical plastic bottles (diameter = 30 mm, length = 60 mm) filled with baby oil (Johnson & Johnson, Skillman, NJ) were fixed around the heel in the RF coil and used as the external proton density reference. The proton density of the baby oil (mineral oil) was calibrated with a plant oil using the MRI system, because its proton density is very close to that of human yellow bone marrow (8).

Three two-dimensional (2D) single spin-echo sequences (TR/TE = 1200 ms/12 ms, 1200 ms/96 ms, and 200 ms/12 ms, slice thickness = 15 mm, FOV = 128 mm × 128 mm, image matrix = 128 × 128, NEX = 1, signal bandwidth = 25 kHz) were used to measure T₁, T₂, and the density of the bone marrow protons in the sagittal cross-sections of the calcaneus, along with the external oil phantom. The total measurement time for the three 128 × 128 pixel images was approximately 3 minutes, because only 64 low-frequency phase-encoding signals were measured, and the k-space data zero-filled to 128 samples. Relaxation

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times and TBVF were calculated in a 20 mm-diameter circular ROI in the calcaneus as described previously (10,11). The speed of sound through the calcaneus was measured using a commercially available QUS instrument (DM-US100: Panasonic, Japan).

Associations between the various parameters were tested using Pearson’s correlation coefficient, and \( P < 0.05 \) was considered significant.

**RESULTS AND DISCUSSION**

Figure 1 shows a typical 2D cross-section and ROI used for TBVF and relaxation time measurements. The diameter of the ROI was 20 mm. Figure 2 shows spin-echo time dependence of image intensity of the calcaneus of the male subject averaged over the ROI. Although several chemically nonequivalent protons contribute to image intensity in the ROI (12–14) and signal modulation caused by J coupling can affect signal decay, this graph demonstrates that most bone marrow protons in the calcaneus undergo relaxation with a single-exponential time constant.

Table 1 shows correlation coefficients (R) between age, SOS, TBVF, \( T_1 \), and \( T_2 \), calculated for the 100 female volunteers. The largest correlation (\( R = 0.90 \)) was that between \( T_1 \) and \( T_2 \), shown also in Figure 3a. This suggests that the major relaxation mechanism is common to \( T_1 \) and \( T_2 \), probably caused by motion of lipid molecules in the bone marrow (15). As shown in Figure 3a, although most of the data points fall into a narrow range of \( \pm 10\% \) from the mean, two outliers of unknown etiology can be observed.

The second largest correlation (\( R = 0.67 \)) was that between TBVF and SOS, as shown in Figure 3b. This fairly

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<th>Parameter</th>
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<tr>
<td>AGE</td>
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<tr>
<td>SOS</td>
<td>( 0.67 )</td>
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<tr>
<td>TBVF</td>
<td>( -0.062^c )</td>
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<tr>
<td>( T_1 )</td>
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<td>( T_2 )</td>
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\( ^a P < 0.0001. \)

\( ^b P < 0.002. \)

\( ^c \)Not significant.
high correlation confirms that SOS is highly correlated with the TB density (16). The correlations between TBVF and age, and between SOS and age, were both negative (−0.48 and −0.56, respectively), which demonstrates that aging process is clearly detected by TBVF and SOS.

It is remarkable that neither T1 nor T2 was correlated with TBVF (\(R = 0.062\) and \(R = 0.024\), respectively), but they showed significant positive correlations with age (\(R = 0.40; P < 0.0001\) and \(R = 0.31; P < 0.002\), respectively), as shown in Figure 4 and significant negative correlation with SOS (\(R = −0.38; P < 0.0001\) and \(R = −0.38; P < 0.0001\)). Because the relaxation times were not correlated with TBVF, the association between the relaxation times and SOS suggests that the former are affected by acoustic or elastic properties of the bone marrow by means of molecular motion. Therefore, the age dependencies of the relaxation times may be caused by molecular dynamics of the bone marrow, which may vary with age.

Figure 5a,b shows temporal changes in T1 and T2 of bone marrow protons measured after the right foot of the male subject had been cooled in ice water for approximately 15 minutes. These findings suggest that the relaxation times increase with heel (bone marrow) temperature, although this could not be determined independently. Figure 5c shows the correlation between T1 and T2 measured in the temperature recovery process. This graph clearly shows that T1 and T2 are governed by viscosity of the bone marrow (15), because this varies with temperature. However, because the variations are approximately 10% even for this extreme case, the nearly double magnitude of ±10% variation in the relaxation times observed for the 100 female subjects cannot be explained by possible temperature variations in the heels of the subjects. Therefore, the variation of the relaxation times must be explained by some mechanism other than the heel temperature.

Red marrow is progressively replaced by yellow marrow in the peripheral skeleton from the birth to adulthood, and
bone marrow in the calcaneus of adults is pure yellow (12,17). Therefore, almost all the NMR signal measured in this study must have come from yellow marrow protons (13,14). To the best of our knowledge, the age-dependent increase in the relaxation times of yellow marrow protons is a new finding. However, the mechanism underlying this process remains to be elucidated.

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REFERENCES